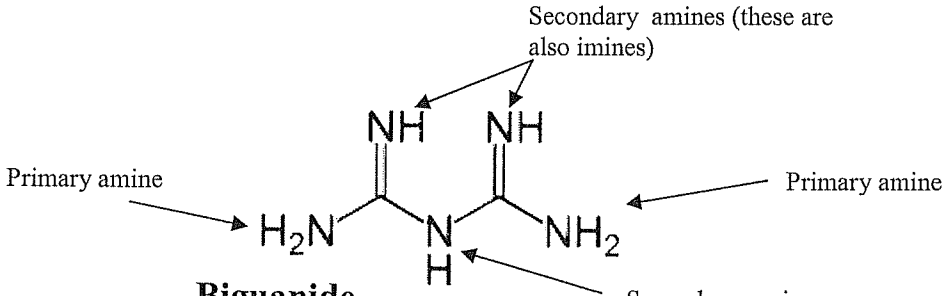
REMARKS

Claims 39-67 are pending. Claims 44-65 were withdrawn by the Examiner after traversal.

Claims 39-43, 66, and 67 stand rejected under 35 U.S.C. §103(a) in light of U.S. Pat. No. 5,142,010 (Olstein) in view of U.S. Pat. No. 5,451,424 (Solomon) and Ikeda et al., New Polymeric Biocides (August 1984). This rejection is traversed. The following remarks are applicable to all of the claims.

A *prima facie* case of obviousness requires all of the claimed elements to be taught in the prior art. But it is respectfully submitted that the rationale does not explain how all of the claimed elements are found in the prior art. In particular, reaction of one of the secondary amine sites of biguanide is never provided. Secondly, the prior art provides secondary amine linkages but not the claimed linkages. Thirdly, the claims require binding through some but not all of the secondary amine nitrogen atoms of the biguanide group. As a fourth dispositive grounds of traversal, the rationale requires an artisan to modify the primary reference (Olstein) in a manner that is not reasonably possible because Olstein can not use the chlorhexidine as proposed by the Examiner; the rationale thus errs by changing the principle of operation of Olsten. As explained below, the claimed invention departs from merely substituting or combining prior art elements, or using known methods, to obtain a predictable result.

Biguanide has primary amines and secondary amines: their locations are illustrated below. As is evident, chemically altering an amine that is at one of primary amine positions does not move the nitrogen at the primary amine position to a secondary amine position.



Biguanide

FIGURE A

As per what is claimed, the Application teaches that some but not all of the secondary amines are to be reacted (see page 8, line 15; page 15 line 19-30; page 20 line 1 to 5 of the attached application). The rejection does not squarely address this feature; it is respectfully submitted that the rationale does not provide reasons that show why some but not all of the secondary amines are reacted. This fact alone is dispositive in favour of allowance of all the claims.

The Examiner's rejection firstly refers to the teaching of Olstein which does, indeed, as the Examiner has said, refer to a polymeric compound with pendant biguanide groups. Applicant acknowledges that the polymer formed will have anti-microbial characteristics (col 3, line 44).

It is important, however, to distinguish between the monomer and the polymer described in the Olstein patent. It is the monomer not the polymer which is useful in the manufacture of bulk polymer, copolymers etc (col 3, line 52-54) and it is the polymer which can be used in various applications, for example medical devices.

The Examiner states that "the reaction sites binding to the polymer include isocyanate" but, with respect, this is not correct. A careful reading of the Olstein passage to which the Examiner refers (column 2, lines 56-60) reveals that the polymerizable group A may contain a

polymerizable active hydrogen containing group such as alkoxy silane moieties or isocyanate moieties. This is the group which makes the monomer A capable of being polymerised. It is not the linker between the monomer A and the pendant biguanide.

In summary, Olstein teaches a polymer which has pendant single biguanide moieties attached to the polymer backbone. These pendant biguanide moieties are linked to the polymer backbone via a secondary amine group.

Therefore, the polymer of Olstein differs from that of the present claim 39 in that each pendant biguanide moiety contains only one biguanide group whereas the polymer of present claim 39 has pendant biguanide-containing moieties comprising a plurality of biguanide groups.

Furthermore, in the polymer of the Olstein patent, the biguanide groups are attached to the backbone via **a secondary amine linkage** whereas in the present claim 39, the biguanide-containing moiety is attached to the polymer backbone via a substituted urea, substituted thiourea, N,N-disubstituted amide, N,N-disubstituted hemiaminal or aminal linkage, or a tertiary amine linkage.

Indeed, the Olstein patent uses **a primary amine site** of the biguanide to make the reaction. But what is claimed is a linkage via a nitrogen atom of **a secondary amine site**. Ikeda also fails to teach this feature. And Solomon does not even chemically react a biguanide. The lack of this claimed element is, of itself, dispositive in favour of allowance of the claims.

The chemistry described in the Olstein patent is such that the method described could not be adapted so as to produce the polymer of present claim 39. This is because, as described at columns 5 and 6 of the Olstein patent, the monomer is formed by reacting a mono or di-amine with a dicyanamide salt to give a monguanido compound of formula (III) followed by further reaction with an amine (e.g a compound of formula (IVa) or (IVb)) to give a biguanide (formula (Va) or (Vb), where Z may be any number of species but is generally a phenylene with a polymerizable species A attached thereto (VIII) (see column 7, lines 8-10). Because the

biguanide is formed in this way, it would not be possible to adapt the chemistry described in the Olstein patent to give a biguanide-moiety containing a plurality of biguanide groups. Nor would it be possible to adapt the chemistry so as to obtain a monomer in which the biguanide-containing moiety is linked to the polymerizable group via one of the linkers specified in present claim 39.

Next, the Examiner states that the Solomon patent discloses a biguanide polymer comprising chlorhexidine. Applicant is referred in particular to the abstract, which does indeed refer to an anti-infective medical article having chlorhexidine bulk distributed through a polyurethane base layer. It is worth noting that the abstract does not say that the polymer comprises chlorhexdine but that the chlorhexidine is distributed throughout a polyurethane base layer. Further, the abstract states that the invention includes a method for preparing the article wherein a homogeneous melt of polymer and chlorhexidine is prepared. This is further amplified in the summary of the invention (column 2, lines 35-45) which states:

> "A method for preparing an anti-infective medical article includes preparing a homogeneous melt of a substantially hydrophilic polymer and an anti-infective agent and extruding the melt through a die to form a medical article having the anti-infective agent distributed substantially evenly throughout the bulk of the polymer (hereinafter referred to as bulk distributed."

Thus, what is disclosed is a physical mixture of a polymer and chlorhexidine. The Solomon patent does not teach a polymer into which chlorhexidine is chemically incorporated.

The Examiner argues that polyurethane is one of the many polymers used in grafting the biguanides of the Olstein patent and therefore a skilled artisan would be motivated to include the biguanides of the Solomon into the preparation of Olstein.

However, Applicants stress that even if the skilled artisan were to combine the teachings of Olstein and Solomon in this way, they would not achieve the product of present claim 39.

Solomon teaches one of skill in the art to melt a biguanide such as chlorhexidine and a polymer. If that skilled person were to choose the polymer of Olstein then the product would be a physical mixture of the polymer described in Olstein and chlorhexidine. A polymer according to claim 39 cannot be achieved by combining the Olstein and Solomon.

The polymer of claim 39 is not a physical mixture of a biguanide and a polymer; it is a polymer with pendant biguanide-containing moiety, wherein each biguanide-containing moiety comprises a plurality of biguanide groups and is chemically bound to the polymer chain. Such a polymer could not be obtained by melting chlorhexidine with the polymer of Olstein.

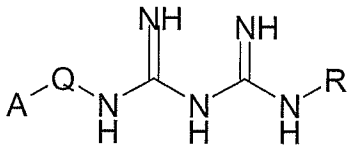
Furthermore, as pointed out above even if a skilled person had been motivated to incorporate chlorhexidine into the polymer of Olstein, this would not have been possible. The method used to prepare the monomer of Olstein, cannot be adapted to prepare a polymer according to claim 39.

The Examiner discusses the tertiary amine group which, it is said, would be an inherent product of the polymerization process if the two references were to be combined. This is, with respect, not the case.

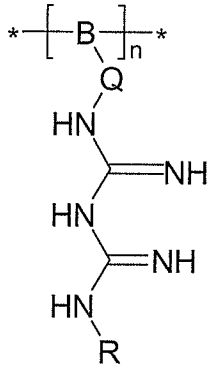
The Olstein patent teaches the formation of a linker attached to a biguanide-containing moiety which has a single biguanide group. It would not be obvious to one of skill in the art how this biguanide could be replaced with a biguanide-containing moiety having multiple biguanide groups, such as chlorhexidine or polyhexanide because the principle of operation for forming the monomer would have to be altogether discarded. A rationale is deficient when it relies on discarding the principle of operation of a reference: this point, by itself, is dispositive for allowance of the claims. See In re Ratti, 270 F.2d 810, 813 (CCPA 1959) (suggested combination of references would require a substantial reconstruction and redesign of the prior art as well as a change in the basic principles under which the prior art was designed to operate). See also, by way of example and not for precedent, the Board's recent opinion in: Appeal 2008-

4305, Application 10/792,108, September 24, 2008 ("replacing the [prior art] Petlyuk tower's prefractionator with a flash drum renders the [cited prior art reference] Petlyuk towers inoperable as a thermally coupled system and changes their principle of operation").

Furthermore, in the monomer of the Olstein patent, the biguanide moiety is linked to the polymerizable moiety via a linker, Q (column 2, structure (II)) or Z (column 5, structure (VIII). Q and Z are said to be "any number of species" but the only example given is phenylene with a polymerizable species A attached (see column 2, line 56 and column 7, line 9). Thus, in the monomer, the biguanide is linked to the polymerizable moiety A as follows:



where Q is phenylene and A is the polymerizable moiety. The –NH-Q- linker could be regarded as a secondary amine linkage. However, when polymerisation takes place, this linkage will remain unchanged. It is the group A which is polymerized and the biguanide remains unchanged. Thus the polymer is of the form:



Where B is the polymer chain formed from A. It can be seen that the linkage between the biguanide and the polymer is not changed by the polymerization process and that no tertiary amine group is formed.

As mentioned above, any isocyanate group which may be present in the monomer would not be present in the polymer as this is the polymerizable group which is chemically converted in the polymerisation process. Thus, if the isocyanate group of Olstein were to be involved in linking the biguanide to the chain, it would not be possible to form a polymer because there would no longer be a polymerizable group in the molecule.

In summary, the teaching of the Olstein patent relates to a polymer with pendant biguanide chains, each pendant moiety comprising a single biguanide group and being linked to the polymer chain via a –NH-phenylene- linker. The Solomon patent relates to a physical mixture of polyurethane and chlorhexidine. One of skill in the art wishing to combine the two would contemplate only melting chlorhexidine with the polymer of Olstein. Even if a person of skill in the art were to be motivated to try to substitute the biguanide moiety of Olstein with chlorhexidine or polyhexanide, this could not be achieved because the chemistry in Olstein can not reasonably be adapted to give the product of present claim 39.

Finally, the Examiner has referred to the newly cited Ikeda *et al* document saying that it discloses biocidal polymeric biguanide compounds comprising pendant biguanides that are linked using secondary amines such as piperidine rings. The Examiner refers in particular to the abstract and to Figure 1 but, with respect, Applicant can find no reference to a piperidine linker in either of these parts of the reference.

Figure 1 illustrates monomers with pendant biguanide moieties. The biguanides are linked to the monomer via a –NH-phenylene- linker which is very similar to that described in the Olstein patent. Indeed, the method for forming the monomers of Ikeda *et al* is extremely similar to that set out in the Olstein patent and therefore, for the same reasons as set out above for the

Olstein patent, the record does not show how a person of skill in the art would be able to adapt the teachings of Ikeda *et al* in any obvious manner to arrive at the polymers of claim 39.

In summary, claim 39 relates to a polymeric material comprising an infection resistant biguanide-containing moiety pendant to a polymer chain. This much is, indeed, disclosed in the Olstein patent and in Ikeda *et al*. However, the claim also specifies that the pendant biguanide-containing moiety comprises a plurality of biguanide groups. This feature is not disclosed in any of the cited documents. Furthermore, as set out above, because of the way in which the monomers are formed in Olstein and in Ikeda *et al*, an artisan can not be expected to produce a polymer with this feature using either of these documents as a starting point.

Next, the claim specifies that the biguanide-containing moiety is chemically bound to the polymer chain through some but not all of the secondary amine nitrogen atoms of a biguanide group. This is certainly <u>not</u> a feature of Solomon, which relates to a physical mixture of a polymer and chlorhexidine. It is a feature of both Olstein and Ikeda *et al* but neither Ikeda *et al* nor Olstein disclose a polymer in which the chemical binding is via a substituted urea, substituted thiourea, N,N-disubstituted amide, N,N-disubstituted hemiaminal or aminal linkage or a tertiary amine linkage. Furthermore, because of the way in which the monomer is formed in both Olstein and Ikeda *et al*, a person of skill in the art would not consider using one of these documents as a starting point for producing a polymer in which a pendant biguanide-containing moiety is linked to a polymer backbone via one of these linkages. A particularly significant point is that the biguanide moiety of Ikeda *et al* and Olstein contains an -NH- group, whereas in the moiety of the present invention there is no hydrogen and the biguanide nitrogen is linked to both the polymer backbone and, directly or indirectly to another biguanide moiety.

In view of this, it is submitted that the pending claims are both new and non-obvious in the light of the prior art.

The Examiner is invited to telephone the undersigned if the Examiner believes it would be useful to advance prosecution.

Respectfully submitted,

/Curtis B. Herbert/

Curtis Herbert, Ph.D., Registration #45,443

Customer No. 62274
Dardi & Associates, PLLC
US Bank Plaza, Suite 2000
220 South 6th Street
Minneapolis, Minnesota 55402
Telephone: (612) 605-1038